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Modelling the glycocalix-mediated transmission of hemodynamic shear forces to the endothelium: a multiscale study

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Introduction

The endothelial glycocalyx (GC) has been identified as the mechanosensor of the forces exerted by the streaming blood onto the vascular endothelial lining [1]. These forces are involved in the focal development of atherosclerosis, and are transmitted to the endothelial cells (ECs) cytoskeleton through the transmembrane proteins, i.e. the terminal structures of the GC layer on the ECs side. Although the relationship between altered ECs gene expression and protein production, and disturbed shear has been extensively studied [2], the mechanisms by which fluid shear forces are transmitted through the endothelial transmembrane anchoring structures is still relatively unexplored. In this study, a multiscale approach is applied to analyze how fluid shear forces are transmitted to the ECs transmembrane anchors through the mechanical response of the GC layer.

Methods

Image-based computational hemodynamics was performed to obtain wall shear stress (WSS) vector time histories in the carotid bifurcation. Realistic atheroprone and atheroprotective WSS vector time histories, as obtained from computational hemodynamics, were prescribed to the modelled GC structure, and the dynamic forces transmitted to the anchoring elements on the EC membrane were evaluated. In detail, the endothelial GC was modelled using the Timoshenko beam theory, and GC deflection and reaction forces in the anchoring structures were gathered. In order to simulate GC mechanical response to fluid stimuli, the Timoshenko beam theory in 3D was numerically solved by using the finite element method-based commercial software ABAQUS. Fluid stimuli $\mathbf{F}_{shear}$ (as the force derived from the WSS vector applied to the surface of GC), and mechanical forces $\mathbf{F}_{mem}$ at the GC anchor point on the EC membrane were calculated throughout the whole luminal surface of the carotid bifurcation. In analogy to the oscillatory shear index (OSI), a measure of WSS multidirectionality, we introduce here the indicator Oscillatory Force Index (OFI), measuring the oscillations of force $\mathbf{F}_{mem}$ transmitted by the GC to the EC membrane.

Results

Discrepancies between OSI and OFI distributions were observed (Fig. 1) in the bifurcation region. Moreover, it was observed that the cycle-averaged value of $\mathbf{F}_{mem}$ in the bifurcation region was similar to the distribution of the fluid shear force $\mathbf{F}_{shear}$. These findings suggest that the GC layer does not merely transmits near-wall forces to the EC membrane as they are, but the GC mechanical transmission modifies the sensed pattern of blood shear forces, especially in terms of direction.

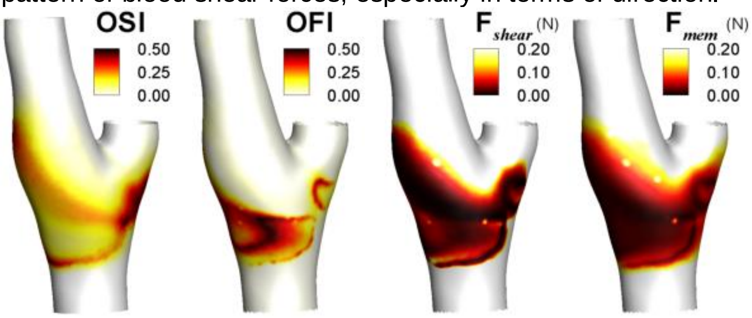

Figure 1 – OFI, OSI, and cycle-average $\mathbf{F}_{shear}$ and $\mathbf{F}_{mem}$ distributions at the luminal surface of the carotid bifurcation.

Conclusions

The proposed approach could contribute to clarify the mechanisms of transmission of local near-wall fluid forces to the ECs, thus bridging the gap of knowledge still existing. In particular, it could represent a powerful tool to link hemodynamics to the mechanobiology of the endothelium.

References

[1] Weinbaum S et al, *Proc Natl Acad Sci*, 100: 7988-95, 2003. [2] Chiu JJ et al, *Physiol Rev*, 91:327-87, 2011.